QUANTITATIVE RELATIVE RANKING:

AN IMPLEMENTATION APPROACH FOR

CALIFORNIA AB1879

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Foreword

Many regulatory agencies across the US and across the globe are considering how to begin the daunting task of assessing the safety of chemicals in consumer products. Industries, academics, model builders and many stakeholder groups have joined the conversation. Hundreds of chemicals must be considered as functionary ingredients of thousands of types of products.

California is on the forefront of such efforts to move to 'greener' chemistry and improve consumer product safety, Laws passed in 2008 (AB1879/SB509) are key parts of the effort which comes at a time when the necessary sciences have evolved to accommodate the challenge, models have already been conceived and tested and necessary information is becoming readily available. In short, the legislative challenge can be met and can be successful with good science, consistent and transparent regulatory implementation and cooperation by all parties in the best interest of public and environmental health

This paper has been developed by The LifeLine Group[1], summarizing research and concept development it has accomplished over the past seven years, much of which was in collaboration with Health Canada for its Canadian Environmental Protection Act. Support for this paper was provided by the Grocery Manufacturer's Association Contacts for further information:

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[1] The LifeLine Group, Annandale, Virginia www.TheLifeLineGroup.org A non profit organization dedicated to improving exposure assessment sciences and their application in the public interest.

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California AB1879 requires ‘greener’ chemistry and improved consumer product safety implemented under standards of good science, prioritization logic, and practicality Recognizing that its goals are common to other efforts globally, it requires consideration of efforts by others to provide experience and information which can inform design of the regulatory process and the assessments. The law requires prioritization to identify problem chemicals and products which then must be addressed by industry. This prioritization must consider both hazard and exposure with capacity to focus on sensitive subpopulations and environmental receptors.

Responding With A Practical Approach

This paper describes a quantitative, exposure-based approach to prioritization to meet that mandate of AB1879. The approach provides a relative ranking of chemicals and products containing those chemicals based on the potential to present significant health threat or environmental damage. The approach is new, but not difficult, operating on a concept of Sentinel Products for groupings of products in the health prioritization. Although this requires new thinking by regulatory scientists, the paradigm is mature and consistent with product manufacturing and retailing realities for which there is abundant information. From both the health and environmental ranking, the DTSC can select those chemical/product groups for attention by the industry as defined in the legislation. Drawing on experience with this approach and the assessment model as employed by Health Canada, DTSC can anticipate modest required resources as compared to traditional chemical regulatory approaches, and can utilize the growing reserves of publicly available chemical-specific and product-specific information from government, industry and other interest groups. This approach meets the prioritization mandates of AB1879 as it enables DTSC to address the highest concerns, selected to fit within available Department resources. It is mindful of the all California business as it presents clear, quantitative, transparent and scientifically based assessments to which industry can respond. It is conservative in its approach, providing the assurances to the public that significant health issues and environmental threats are, indeed, being identified as intended by the legislation.

This document presents an overview of the approach. Much more detail and the prioritization model can be made available as well.

1. Background—Setting the stage

The prioritization of chemicals contained in consumer products is one of several core mandates of the 2008 Green Chemistry legislation (AB1879/SB509). The department is directed "*…to establish a process to identify and prioritize those chemicals or chemical ingredients in consumer products that may be considered as being a chemical of concern*". The statute indicates that the process must address: "*(1) The volume of the chemical in commerce in this state, (2) The potential for exposure to the chemical in a consumer product, and (3) potential effects on sensitive subpopulations, including infants and children*". The statute further directs that "*In adopting regulations pursuant to this section, the department shall reference and use, to the maximum extent feasible, available information from other nations, governments, and authoritative bodies that have undertaken similar chemical prioritization processes, so as to leverage the work and costs already incurred by those entities and to minimize costs and maximize benefits for the state's economy*."

Since the enactment of the Green Chemistry legislation, the prioritization mandate has been the subject of numerous workshops, stakeholder comments and most recently in Green Ribbon Science Panel (GRSP) discussions. All stakeholders and the Department[2] have expressed an interest in ensuring that the process identifies and addresses the highest impacts to human health and the environment.

DTSC[3] recently summarized the factors that might be considered in prioritization for chemical hazard (extent to which chemical exhibits one or more hazard traits, toxicity, potency, effects on sensitive subpopulations and environmental receptors, *etc*.) and chemical/product exposure (volume of the chemical in commerce, types of products containing the chemical, mode of application of the products, concentration of the chemical in the products, frequency and duration of use of the products, potential exposure scenarios and pathways for sensitive subpopulations and environmental receptors, magnitude, extent and impact severity of likely exposures and the product's relative contribution to the concerns related to the chemical, *etc*.). These are all important and scientifically robust considerations for making prioritization decisions.

In drafting proposed regulations, DTSC identified criteria that would be the basis for prioritization decisions:

[2] The legislation assigns authority to California's Department of Toxic Substances Control (DTSC).

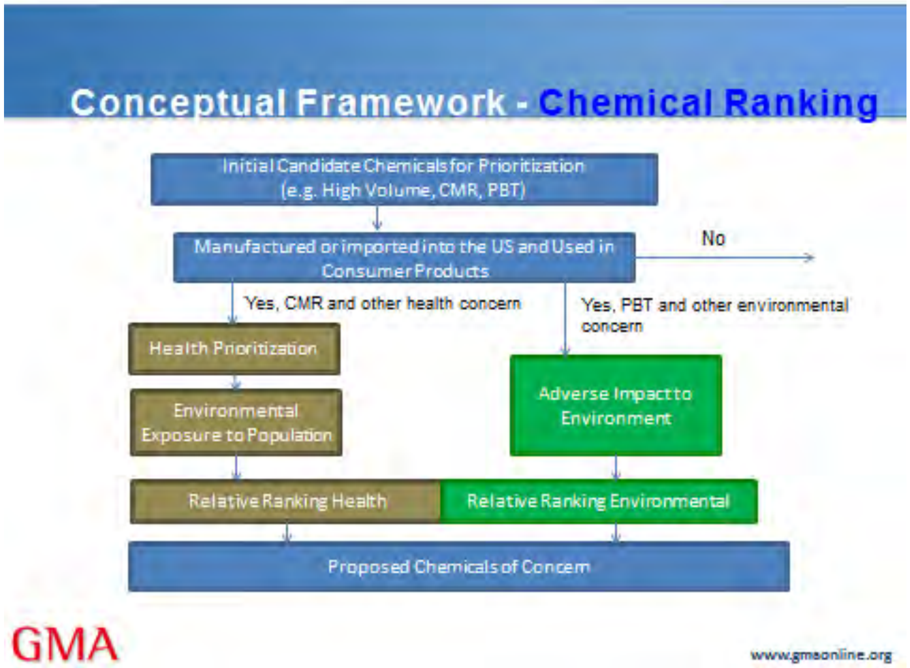
[3] Regulatory Concepts for Chemical and Product Prioritization 5-03-2011" summary by DTSC for the Green Ribbon Science Panel

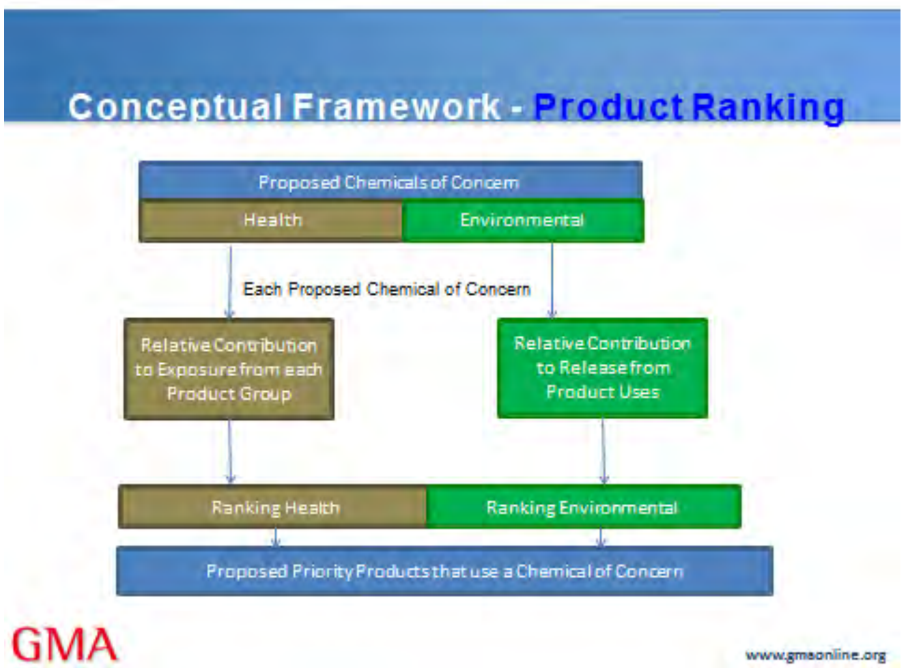
- "*…the greatest potential for consumers and environmental receptors to be exposed to the chemical in quantities that can result in adverse public health or environmental impacts*."
- "*…the greatest potential for public and the environment to be exposed to the Chemical of Concern contained in the product in quantities that can result in adverse public health or environmental impacts*."
- "*…the availability of Department resources*"

All of the above presents a significant challenge to the Department. There may be hundreds of potential chemicals of concern, which are used as ingredients in thousands of potential priority products. The prioritization criteria and factors for decisions noted above necessitate a quantitative approach to prioritization. While qualitative factors such as indications of presence in biological or environmental media and presence in consumer or sub-population products can be useful for initial screening to identify a pool of candidate chemicals or a pool of candidate products using the chemicals, these are binary factors (i.e., Yes/No) and cannot be effectively and meaningfully used in a scientific prioritization process. A quantitative prioritization process is essential to address the above prioritization factors and to establish the scientific basis for prioritization decisions within the scope of available Department resources.

The framework for the quantitative chemical and product prioritization process to meet these criteria is shown in Figure 1. In the first step of the prioritization, an initial pool of candidate chemicals is identified for prioritization based on chemical volume and other indicators of exposure (such as biomonitoring and environmental monitoring data) and on chemical hazards including those that impact sensitive subpopulations. For example, those categorized as PBT—Persistent, Bioaccumulative and Toxic or the CMRs – Carcinogens, Mutagens and Reproductive Toxins could be candidate chemicals. There are a number of federal and international authoritative sources that can help to identify chemicals with these properties. These candidate chemicals are further narrowed based on manufacture/import and use in consumer products in the U.S. Chemicals with health concerns (e.g. CMR) are ranked for adverse health impact based on direct exposures from products as well as indirect exposure to the population via the environment. Chemicals with environmental concerns (e.g. PBT) are ranked based on adverse impact to the environment. DTSC would use the Health and Environmental chemical rankings to select proposed chemicals of concern. In the second step of the prioritization, product rankings are developed based on the relative contribution to human and environmental exposure from the products that use the proposed chemicals of concern. DTSC would use the health and environmental product rankings to select proposed priority products that use a chemical of concern. The details of how the health, environmental chemical and product rankings are developed are described in the remainder of this document.

Figure 1: Conceptual Prioritization Framework





2. Prioritizing Chemicals and Products for Health

"Prioritization based on potential adverse public health impact" is an important component of proposed regulations in California. Prioritization in this context means setting up an order for thorough assessment …doing the "worst first". The question becomes one of knowing which could be "the worst", identifying areas where significant improvements could be most effective, before moving on to undertake the arduous alternative assessment.

So, the objective is to first from a large set of candidate chemicals that are used as ingredients for different functions in widely divergent types of products, rank the chemicals as to their probability to cause adverse impacts to different subpopulations that may use those products. Then, for those chemicals that present the greatest potential for adverse impact, identify those products contributing the greatest proportion of the impact.

The regulation also **requires a practical and meaningful process** be employed that accomplishes the goal of the legislation with an efficient government approach that evokes a constructive, meaningful response from manufacturers of consumer products. Drawing on the lessons from other regulatory processes, achieving "practicality" will require something new.

In this section of the document, we describe a process illustrated in Figure 1, which can achieve the legislative mandate and regulatory concepts discussed previously. This prioritization process has been developed over the past seven years and employs tested techniques and tools. The concept was developed as part of a Health Canada program which also focused on potential for exposure and striving for safer consumer products. As a "road tested" idea, lessons about its advantages and limitations are available for consideration.

This prioritization process is new, but not necessarily difficult. It departs significantly from the more traditional predictive approaches. This is the cornerstone concept and deserves some discussion.

2.1 Basis For Prioritization Process – Exposure

For the California proposed regulation, the key driver for this prioritization is "the potential for consumers…to be exposed to the chemical in quantities that can result in adverse public health or environmental impacts." The determination of "To cause adverse impact" implies a science-based prioritization, utilizing both the potency (hazard) of the chemicals and the exposure to those chemicals via the products under consideration. A significant advantage of this legislation and regulation is the focus on potential for exposure and prioritization at its core. The science, tools and techniques of exposure assessment have blossomed over the past decades making it an equal partner to hazard identification. One of the advantages of exposure assessment is the relatively modest cost required in terms of resources and time for acquiring the basic information on which these assessments are built. Also, the expanding achievements of modeling make the task of prioritization based on exposure practical, meaningful and scientifically credible.

2.2 Principles of Exposure and Hazard Underpinning Prioritization Processes for Health

Exposure assessment and adverse impact assessment are terms, which capture a broad range of objectives, especially within the context of chemicals used in consumer products. There are fundamental differences among available approaches. All approaches are useful for some purposes, but not all are useful for the purpose of prioritization.

Traditionally, some level of <u>predictive exposure and risk assessment</u> is employed for regulation. This approach has many "levels of precision", but fundamentally its goal is to estimate the exposure and estimate the risk presented by a given product or chemical. In some cases, multiple products could be considered simultaneously (true aggregate assessments[4]), and even multiple chemicals across all of their uses might be considered (cumulative risk assessment[5]).

Typical predictive exposure and risk assessment methodology addresses only a single chemical and single product at a time. The values used in exposure algorithm parameters are usually normative—values representing the usual case, averages, medians or even full distributions of values. To reduce the effort level necessary to conduct predictive assessments for many chemicals and many products, "screening level" predictive assessments have been employed. Although these approaches require minimal data, the resulting prediction may be crude and/or overestimate the impact. Summing the resulting screening predictions to represent an aggregation of risk only amplifies the exaggeration. Better precision may be achieved in

[4] Note that an "aggregate assessment" is not a simple summation of a series of single source assessments. That simple summation, while "doable" and tempting, is not scientifically credible and ignores obvious product competition and co-uses by different people across different time periods, etc.

[5] Methods which employ "reference chemicals" and relative potencies across families of chemicals are actually aggregate assessments using a single reference chemical. The rare "true cumulative" assessment tools have not yet been utilized for major regulatory issues.

subsequent assessment with better data and models, but so often the public remembers the first answer and efforts to "reduce the risk value" are criticized and problematic.

Prioritization is different than Prediction. It presents a relative ranking of multiple chemicals and their multiple products, considered simultaneously. The ranking is based on a quantitative process, but the value calculated for any given chemical and product's exposure is NOT predictive and is relevant only in terms of positioning the chemical or product relative to that above or below it in the pool. Relative ranking tools are used for prioritization, but not for exposure/risk prediction. In the relative ranking approach presented here, the model also tracks each product's relative contributions to the overall exposure and adverse impact for a given chemical. In that way, products contributing significant proportions of the overall exposure and impact can be identified.

Prioritization is a relative ranking of chemicals or categories of products based on potential exposure and/or adverse health impact. The actual exposure/adverse impact calculation is NOT predictive and is NOT a screening value.

Prioritization for human health can address whole groups of chemicals and their products simultaneously in a disciplined structured process. The task of relative ranking can be efficient, achieving the objectives of the regulatory mandate while saving resources and time for the subsequent focus on those chemicals and products that are contributing most heavily to the potential public health impact.

The underlying approach of relative ranking entails the following:

- Products and uses are grouped by exposure features;
- One or a few Sentinel Products from each product grouping are chosen because they plausibly represent the greatest exposure scenarios within that grouping. Only Sentinel Products, not all of the products, are utilized in ranking calculations;
- Parameter values used in exposure assessment calculations are maximums (or high end values), not "usual or normative" values;
- Ranking models generate a ranking from high to low in relative terms.

This prioritization approach has some important advantages, including:

- Initial rankings are based on a quantitative methodology but the quantitative assessments are not assumed to be predictive assessments. From the relative ranking, chemicals (or products) can be advanced for further scrutiny or reserved for later attention.

- Relative ranking operates on limited, but decision critical, amounts of data.

- Exposure scenarios for entire groups of products can be efficiently addressed**.** Also, entire groups of chemicals can be efficiently assessed.

- The approach is conservative, using high-end values, not normative values in the calculations.

- It is responsive to the requirement for focus on sensitive subpopulations, hazard-based criteria and other legislative requirements.

2.2.1 Potential for Exposure

Potential for exposure is the pivotal parameter for priority setting. And, a relative ranking approach based on potential for exposure will address important (and practical) elements such as:

- Probability chemical might be in the products which includes consideration of chemical function/price/manufacturer/country of origin/target consumer,

- Type of Product: Products can be grouped by exposure potential,

- Use profiles of products including frequency of use, concentration of the chemical in product,

- Subpopulations…most exposed and most vulnerable.

Probability chemical might be in the products: Chemical ingredients serve a function within each consumer product such as a colorant, plasticizer, barrier, softener, sealant, adhesive, fire retardant, etc. In some cases, multiple chemicals may serve the same function to different degrees of performance. The price, manufacturing practicalities of the consumer product, countries of origin and target consumer are factors that influence the probability that a given chemical will be in some or all of a given type of product. The choice of chemicals for each functional ingredient within the consumer product influences performance, item price, market availability and aspects of use of the product. Using public information sources, one can learn about the functional properties of a chemical and thereby its likely concentrations in different kinds of products.[6] Upper bounds of those concentrations are applied to the calculations in keeping with the principles of the ranking scheme. Note that understanding functionality of chemicals as ingredients in a product is a new topic for many assessors and thus will require some initial effort to understand. The utility of the concept makes that learning task worthwhile, however.

Type of Product: As part of the task to prioritize the products and chemicals in terms of exposure potential, it is important to consider the potential for exposure which depends on the type of product. Think of all of the products in a hardware store, an electronics store, a salon, a department store, etc. How could the thousands of products be categorized based on exposure principles? For illustrative purposes consider the example of a toy store.

First, we can set up categories of items defined by their exposure potential.

Items such as balls, puzzles and board game pieces would infer exposure opportunities via dermal contact primarily to one side of the hand. For very young children, one could envision mouthing events as well.

Items such as masks and costumes, sleeping bags, and clothing present quite a different opportunity for exposure, especially in terms of body surface involvement and duration of contact.

Paints, modeling clays, or bubble bath solutions set up yet another exposure scenario. The chemical ingredients impinge closely to the skin and may also moisturize the skin during exposure. Duration may vary but the dynamics for uptake of the chemicals from the product are quite different than from the other groupings of products.

Products for infants and young children will require consideration of substantial oral contact or secondary oral contact from toy-to-hand then hand-to-mouth transfers.

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[6] *Using Publicly Available Information To Create Exposure And Risk-Based Ranking Of Chemicals Used In The Workplace And Consumer Products*, Jayjock, Chaisson, Franklin, Arnold, and Price, Journal of Exposure Science and Environmental Epidemiology (2009) 19, 515–524

A wide range of products are used by children to ride on, climb on, sit on, etc. Contact is quite different than from other product groupings and may be brief, involve clothed body areas and rarely direct oral exposure (though possibly secondary oral exposure). An exposure profile for this grouping is also possible to construct, including variations appropriate for different age groups or subpopulations.

In this way, items from the entire store can be placed into a manageable set of product groupings, each with their own common exposure scenarios. Within the groups, values for elements of the exposure scenarios may vary depending on the age group using the item, but such variations are easily accommodated.

Use profiles of products: The understanding of "use profiles" for products is a fundamental part of the exposure assessment. For most products, like household products, cleaning products and personal care products, publicly available information can set up use profiles that are appropriate for different age groups, genders, socio-economic groups or other subpopulations. Exposure assessment scientists are learning to apply marketing data and other business information to questions about how chemicals are used in products and how consumers use those products. This too may be a new topic for most assessors, but the insight provided by this atypical information is valuable and easily attainable. Existing, available information informs us about:

- Frequency of use – may be seasonal, gender, age specific,
- Co-use relationships "If you use lipstick will you use eye liner?",
- Exclusivity by subgroup "If you use lipstick will you use aftershave lotion?,"
- Competitive use relationships "If you use powder detergent will you ALSO use liquid detergent?"

Product groupings can be made, as with the toy example, for which probabilities can be assigned for:

- Probability of use,
- Co-use with other groupings,
- Competitive probabilities with some groupings.

Indeed, use of the products creates opportunity for exposures including the initial exposure to the user, exposures to others within the personal environment area, and exposure to self and others at later times due to residues created in the personal environment. Also, use and disposal of the products may create additional opportunities for exposure via the indirect or secondary environmental route. Exposure through the environment can be considered as a contributing element to the potential for exposure and adverse impact. This is discussed later in this document (Add section number).

For each category one or a few products or types of products can be identified that represent the probable greatest exposure opportunity—in terms of duration of exposure magnitude of exposure to the chemical via inhalation or dermal or oral routes or both duration and magnitude of exposure. These are the "Sentinel Products" which will be used in calculation of the potential for exposure and adverse impact for the chemical which will be discussed in more detail in Section 2.2.2.

Subpopulations…most exposed and/or most vulnerable. Both perspectives accommodated in prioritization mechanics.

Subpopulations…most exposed and most vulnerable: Exposure profiles can be constructed for subpopulations of special interest. Public health legislation and regulation frequently provide for special attention to "most exposed" subpopulations and/or "most vulnerable" subpopulations. These terms are sometimes used interchangeably when indeed they mean very different things.

Most exposed - a function of the person's interaction with the products and media in which the chemical exists. Because of a subpopulation's unique use of a product or duration of use or frequency of use, they may have a much higher exposure profile than people in other subpopulation groups.

Most vulnerable – a function of biology…a person's proclivity to have an adverse effect from a given exposure to a chemical. There is inherent human variability in vulnerability due to age, gender, pregnancy, disease, exposure to other stressors, nutritional status, etc. This can result in different health consequences among people experiencing the same exposure to the same chemical.

The relative ranking prioritization process presented here addresses both kinds of "subpopulations of special interest" within the mechanics of the assessment.

2.2.2 The Sentinel Product

Key to this approach is the "Sentinel Product", so let's consider what this is, and what it is NOT intended to mean. A chemical may be used in literally hundreds of different kinds of products. Different age groups will come into contact with different combinations of these products and under different use profiles. The prioritization assessment will be undertaken in the relative ranking model for each age group and will consider only those Sentinel Products thought to present significant exposure to that age group. Significant may mean high amounts and/or frequent exposure and/or durable exposure and/or exposure under conditions of vulnerability for that age group. The goal is to include all "significant" exposure situations but minimize the overall number of products to be considered by the calculation. Those products to be included are called "Sentinel Products" but that does NOT mean that they have been shown to be dangerous or products of concern. The term "Sentinel Products" is **Not** to be confused with the term "Priority Products" as defined in proposed California regulation as those products thought to present a health or environmental impact due to potential exposure to the product's ingredients.

> The **Sentinel Product** is a type of product from an exposure-based grouping of products which is likely to provide opportunity for the greatest exposure (by duration, frequency or magnitude) to an ingredient chemical by a population group.

The selection of Sentinel Products employs the general principals of exposure:

- o Direct contract is necessary for dermal exposure;
- o Compounds must be volatile or the product must generate respirable particles to result in inhalation exposure;
- o Higher transferable concentrations increase the potential for higher exposure.

- More than one Sentinel Product may be appropriate to represent the most significant exposure potential to a population group for a group of products. This may be especially relevant for products where co-use is prevalent
- Exposure parameters assumed to be the maximum reasonable value for a range of possible values….not the normative value (most common or representative) [e.g. select the high end from a range of concentrations of surfactant in toothpaste]

This last point brings in other important considerations for selecting the Sentinel Products.

1. We know that exposure is NOT proportionately distributed across all subpopulations in the population. In part that is because the opportunities for exposure differ from one group to another and in large part that is because of their use of consumer products and people's activities in their personal environments. This disproportionality is important to consider since the process calls for using the upper end value of any distribution of values.

2. We know that exposure is defined by more than magnitude. Duration, frequency, and route of exposure are equally important to consider. We know that product use varies from period to period for any given individual and it is the degree of that variation that is important to consider. The greater the variation, the more likely that a high-end exposure factor will be important to consider. Seasonality may cause this variation, or perhaps significant variation occurs because of holidays or other short periods where product use and personal activity patterns change.

Choice of Sentinel Products across all product categories is a critical step in the prioritization methodology and warrants a structured approach with defined decision criteria to ensure science-based selections

2.3 Presentation of Approach for Prioritizing Chemicals and Products

The initial influences on candidate chemicals for Prioritization may come from a legislative mandate and/or contemporary concerns about specific chemicals. Historically, production volumes were used to set priorities with an underlying presumption that chemicals of high production volume must be greater contributors to public health and environmental impacts. At least for the public health side of this logic, the presumption has not held up to the facts. So, while volume may be among the useful criteria in identifying candidates for Prioritization, using volume alone to set priorities could result in inaccurate priorities.

Candidates for prioritization could include chemicals known to have significant toxic properties and potencies (hazard), those presenting significant concerns for public health (especially to sensitive subpopulations), air quality, ecology, water or soil.. So, from the tens of thousands of chemicals in trade, it is likely that several hundred (perhaps 100 to 1000) are the most important candidates for prioritization. It would require a massive time commitment and resources to undertake predictive risk assessments for a thousand or even several hundred chemicals. This is where relative ranking can prove most beneficial, highlighting those chemicals and products likely to be the biggest contributors to adverse public health impacts. The resulting ranking of the proposed Chemicals of Concern and the attendant proposed Priority Products in which the Chemicals of Concern are used could be utilized to determine which product and chemical pairs to advance as illustrated in Attachment 1, following public notice and comment. They become proposed Chemicals of Concern and proposed Priority Products because they're at the top of relative rankings based on hazard and exposure potential. The initial candidate chemicals list was driven largely by hazard concerns. The subsequent prioritization assessment is based on potential for exposure and resulting potential for adverse public health impacts. So, if people are likely to have significant exposure opportunities to a potentially hazardous chemical via consumer products, those chemicals and products representing the substantive proportion of the exposure and potential for significant adverse public health impacts will be higher on the relative ranking and become the focus for additional attention.

So, a pool of candidate chemicals manufactured or imported into the US and for which there is a significant hazard potential will undergo a prioritization task where they are ranked as to their potential to cause adverse impacts, using an exposure-based assessment system.

The approach entails:

1. Identifying the functional uses of each chemical and the products in which it occurs,

2. Applying use profiles—mathematical descriptions of how different subpopulations use different types of products

3. From these uses/products, selecting Sentinel Products expected to deliver the most significant (by magnitude, condition or duration) exposure to a given subpopulation. These Sentinel Products will be used in the relative ranking calculation.

4. Applying product use profiles and chemical use information in a relative-ranking model which

    a) Displays the relative order of adverse impact by chemical, and

    b) Displays each product's relative contribution to overall exposure to that chemical.

2.3.1 Types of Information Required

To implement this approach three types of information are required:

- Chemical Specific Information,
- Product Specific Information, and
- People Specific Information.

"Information" could be:

- Precise, relevant data from traditional experimental efforts, monitoring or other structured data-gathering processes;
- Surrogate data, generated for some other, related chemical, product or population group or exposure scenario;
- Derived data, constructed by mathematically "customizing" a data set to make it relevant to the chemical, product or subpopulation parameter where information is needed;

- Default values, providing operational values for required algorithms. Default values may come from anywhere in the information range--experimental data to fact-free assumptions.
- Assumptions, which are judged by common sense and professional judgment when no better source is available.

As with any deliberative process, the better the information, the better the confidence in the final decision. But that does not mean that "perfect data" are required. Indeed, regulatory scientists face this situation many times and have evolved "principles of practice" to determine the required pedigree of information destined to inform different parameters. This will likely be the case here as this process evolves.

Transparency of the prioritization process through review and comment serves a special purpose here. As stakeholders view the information employed in the ranking and consider their sources, they can elect to provide better information to improve the assessment. This normal process of instigating for better information is greatly enhanced by the transparency of the assessment model, its algorithms and knowledge bases.

There are two types of **Chemical Specific Information** – the hazard information and the exposure-related information. The <u>hazard/toxicology information</u> addresses one or more significant health consequences – toxicological endpoints such as cancer, birth defects, reproductive effects, etc. Any chemical could have multiple toxicological endpoints ranging from quite serious to relatively minor, transient effects. A key policy decision will affect any prioritization process—"What health endpoints will be considered "significant" and relevant to the regulation?" Making all toxicological endpoints part of the deliberation, no matter their significance to public health, unnecessarily complicates any prioritization process and its efficiency.

For each significant toxicological endpoint, a potency metric is selected or derived appropriate to long-term (chronic) or short-term (acute) exposure to the chemical, as well as definition of relevant routes for those metrics to apply. (Some chemicals' toxicity is route dependent.) Potency for carcinogens will be converted to a level related to the *de minimus* risk – a probability point determined, again, by policy, perhaps at either the 1/1,000,000 or 1/100,000 probability point. [10^{-6} or 10^{-5}]. Policy declarations will also guide the use of surrogate data and derived information (such as Structure Activity Relationships).

The <u>exposure-related chemical-specific information</u> is simpler and often publicly available. This includes those physical-chemical characteristics that influence the chemical's ability to get into or onto a person's body and travel through the environment. Lipophilicity, molecular size, vapor pressure, reactivity and other such data are usually easy to find, and these chemical properties are usually directly related to their functionality in the product(s). These physical-chemical characteristics are also used in predicting exposure through the environment (Section 3.4)

In general, chemical specific information is just that…applicable only to that one chemical. For some families of chemicals, information about one chemical may inform the search for information about its close relative, but individual chemical information searches are a part of the task. Experience with the resource requirements associated with gathering these types of data are discussed in Section 2.7.1.

The **Product Specific Information** starts with understanding what function the chemical has in a type of product. Is it a surfactant, solvent, emulsifier, stabilizer, colorant, etc? And acting as this kind of ingredient, what is the range of concentrations needed to accomplish that function? This involves understanding how the chemical is used in a product. The second kind of "use" information is how the product is used by different people during different times and conditions. Among the thousands of products, many are competitive but sometime closely tied to co-use scenarios. Increasingly, such information is publicly available as well.

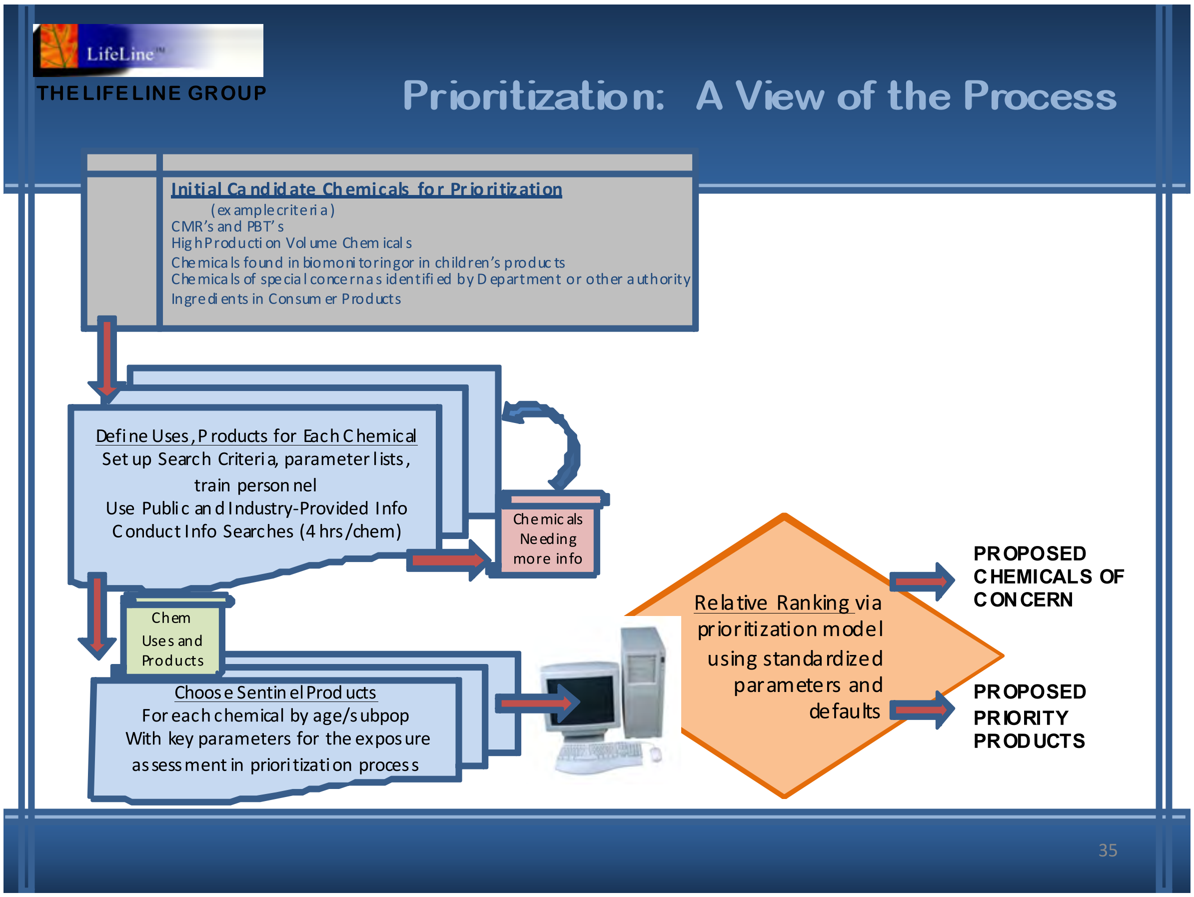
Exposure scenarios of product use, once developed, are applicable to any of the chemical ingredients in those products. In other words, the product use scenarios are "reusable". A catalogue of product use scenarios, along with default data, assumptions and other particulars will accrue as a natural by-product of the process. Capturing the structure of these product use scenarios as they are developed will provide two advantages: significant efficiency in the process and consistency across the DTSC assessors working in the process. A third advantage—transparency—can be accomplished if the use scenarios are catalogued and published for constructive comment.

The **People Specific Information** is independent of the chemical. It is the information that describes the morphometrics, physiology and activities of people. What are their height, weight, breathing rates and surface areas for different body parts? What are they doing in their personal environments that bring them into contact with products and their ingredient chemicals? In other words, what are their activity profiles? All of these things are age dependent, possibly seasonally dependent and frequently dependent on gender, economic and ethnic factors.

Once this information is developed, it is reusable in all subsequent analyses. And this can be constructed from published scenarios developed by public health agencies for related exposure assessment activities. A growing basis of data to inform subpopulation-specific parameters is evolving as well.

2.4 Illustration of Prioritization Approach

A thorough understanding of the relative ranking process requires a far more detailed discussion than possible in this introductory document, but it can be characterized in the following sketch. An illustrative walk-through follows.



2.4.1 Step 1: Candidate Chemicals

From the tens of thousands of chemicals in commerce, a subset of chemicals (perhaps 100 - 1000) would be selected as candidate chemicals based on concerns about significant potential adverse health effects, environmental damage or other contemporary issues such as:

- Production Volume;
- Carcinogens, Mutagens or Reproductive Toxicants (CMRs)
- Other information indicating the potential for significant impacts on public health, especially sensitive subpopulations;
- Chemicals of special concern as identified by Department or other authority.

2.4.2 Step 2: Defining the Uses and Products

Using Publicly Available Information defining Use Profiles for types of products, find the physical/chemical characteristics, functional uses of the candidate chemicals, and the types of products in which they are likely ingredients.

- Chemical use in products is driven by functionality of the chemical (e.g., surfactant, colorant, stabilizer, aromatic) and the cost associated with that chemical for that function.
- Functionality driven by basic physical/chemical properties and this informs initial searches for chemical use in products.
- Publicly available information usually provides good initial information on uses and potential products for consideration.

2.4.2.1 Examples of Publicly Available Data

Successful search strategies are quickly developed by scientists undertaking the information search task, and core searching pathways can be developed for the Department scientists to increase the efficiency and thoroughness of this task. In general, logic and sites as described below are examples of the type that have proven useful.

How are chemicals used in products? Possible health concerns and toxicology reviews:

- Chemical sales literature and safety information (online) by manufacturer (i.e. Dow Chemical)
- Government chemical and product reviews such as http://www.nicnas.gov.au/publications/information_sheets/existing_chemical_information_sheets

Characteristics of the chemical, sources, related information

- US Nat'l. Center for Biotechnology http://www.ncbi.nlm.nih.gov
- Forms, sources, links to other info sites http://www.chemindustry.com

Concentrations in products, possible substitutes, functions in products and use scenarios/profiles

- Government (e,g, US EPA Inventory Update http://www.epa.gov/iur/tools/data/index.html; Household Products Database http://hpd.nlm.nih.gov)

- European evaluations under REACh. 4,000 dossiers available now, including high hazard chemicals and expected to double by 2013.
- The Cosmetic, Toiletry, and Fragrance Association (2006) International Cosmetic Ingredient Dictionary and Handbook, Washington DC, Ed Wenninger JA McEwan GN
- American Cleaning Institute Consumer Product Ingredient Safety 2nd Ed, Washington, DC.
- Cleaning product Ingredients: http://www.cleaninginstitute.org/clean_living/locating_cleaning_product_ingredients.aspx
- Downstream product mfr websites. SC Johnson, Clorox, P&G
- Fragrance ingredient information (> 3000 listed) by IFRA/RIFM http://www.ifraorg.org/en-us/Ingredients_2

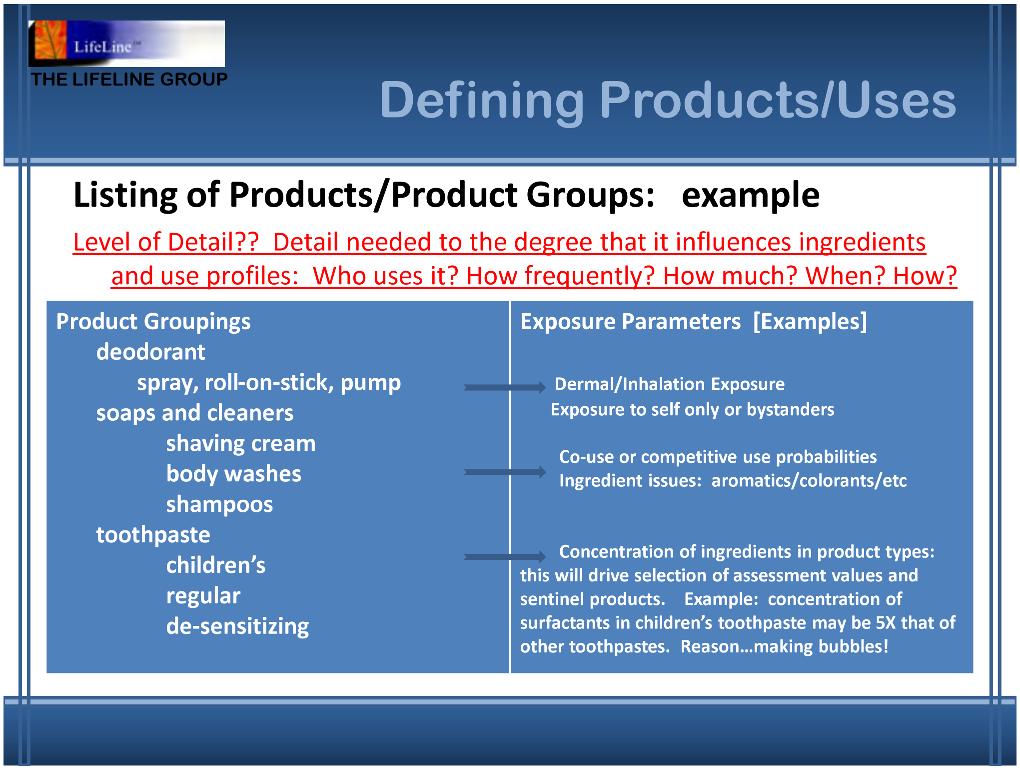
Exposure factors for assessment calculations:

- US EPA Exposure Factors Handbook
- LifeLine™ compendia of activity profiles and dietary profiles
- American Cleaning Institute Consumer Product Ingredient Safety 2nd Ed, Washington, DC.

Part of the objective is to define probable upper bound concentrations of the functional chemical in product types. This can vary depending on the product characteristics desired by the target consumer. Thus a given product type may become a Sentinel Product only for a specific subpopulation because of the high concentration of the chemical in products used primarily by that subpopulation. For example, when bubbles are a desired feature of the product because the target consumer is young children, concentrations of surfactants may be much higher than in similar products marketed to adults.

Next, the resulting set of products is grouped according to exposure-related criteria, including concentration of the chemical in the product, duration and/or frequency of use, and opportunity for dermal contact, ingestion or inhalation. Variability in these factors may be introduced by seasonality, ethnicity and economic situations. Since the prioritization approach operates on upper limit parameters, that variation is important to understand so that upper-end values are chosen OR unique population subgroups are considered in the prioritization logic.

In the illustration below, some personal care products are grouped by exposure-related criteria. The example ingredient is a surfactant and part of the grouping could look like this.



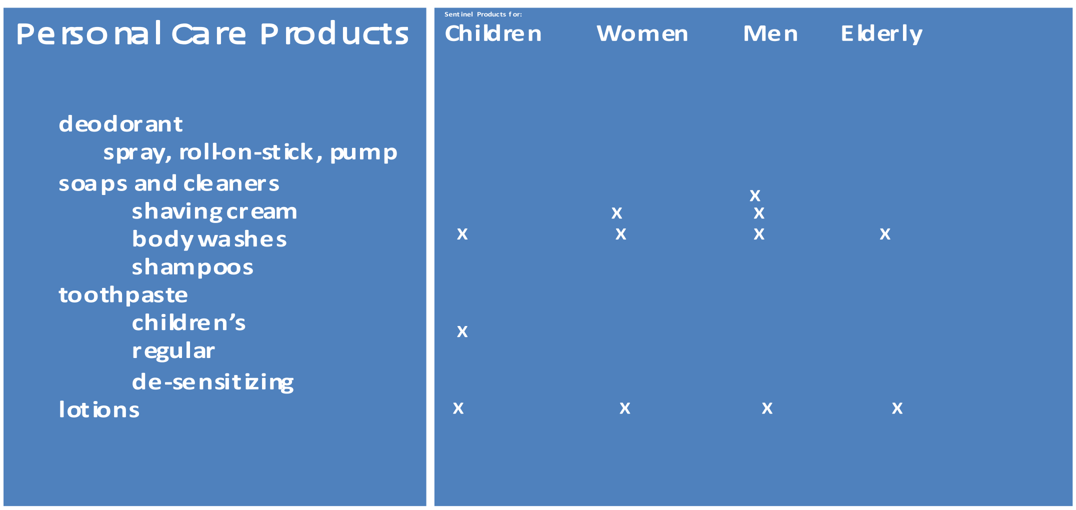
2.4.3 Step 3: Selecting the Sentinel Products and Including Environmental Exposure

For each product grouping, consider selecting one or more Sentinel Products for each age group or other subpopulation of concern. It is not necessary to have a Sentinel Product for each age group or subpopulation, and multiple Sentinel Products may be appropriate for some product groups. These decisions are based on exposure potential and the likelihood that a product type could set up an opportunity for a comparatively high level of exposure to a given subpopulation by one or more routes.

Here is where the consumer's product use profiles are linked to probable degree of exposure considering concentration of the chemical in the product, duration and frequency of use, potential for contact, ingestion or inhalation. Usually, but not always, higher concentrations of the chemical in a product increase the potential for a higher human dose. For any age group, there may be multiple products that can present significant exposure opportunities in terms of amount, duration, or frequency. All of these products should be included as Sentinel Products.

Selection of Sentinel Products should proceed through a disciplined deliberative process with structured criteria consistently applied by all assessors. In addition to reducing reviewer bias, the criteria can reflect Department policy about degree of conservatism, completeness, and dealing with variability and sensitive subpopulations.

In our illustration, we consider a chemical with amphiphilic properties. Its chemistry creates an excellent anionic surfactant and properties required in detergents, paints cosmetics, and craft products. It functions to make bubbles, dissolve grease and helps to keep other ingredients into a smooth solution. Our illustrative chemical is inexpensive and exists in many different products serving those functions. It could be a frequent ingredient in children's products (anything involving bubbles and many art supplies), cleaning products, personal soap products or toothpaste. Depending on the desire for bubbles or the needed strength of the detergent



and grease-cutting challenge, the concentration in the product will vary.

Consumer's uses of these kinds of products will vary with age, so the choice of Sentinel Products could certainly be different for different age groups as illustrated in the following figure. For example, for young children, their exposure to the surfactant could be from hand soaps, bath soaps and bubble soaps (all with dermal and some oral exposure), art products and bubble toy products (dermal and incidental oral), and possibly from residues of the chemical in clothes, bed clothing or other household cleaning products. The concentration of the chemical in children's toothpaste (higher than in adult's toothpaste) and variability in amount used and amount swallowed makes toothpaste a good candidate Sentinel Product for children but not for adults. Bubble bath and body wash products can be considered as a Sentinel Product. Again, variability in the use profile and high concentrations of the chemical in these products make it a candidate Sentinel Product.

The selection process for adults yields different Sentinel Products. In de-greasing hand soaps a very high concentration of the surfactant is needed. The concentrations in some of these soaps are ten-fold higher than in regular personal care soaps. Use of these products may be rare for most people, but for those with hobbies involving machines, bearings, engines or many different types of art, these soaps are popular and frequently used.

For most adults, a daily full body exposure to a 5% soap product in a 15-minute bath or shower would suffice as one Sentinel Product and a second daily exposure is expected from the use in shaving cream. An important difference is that for men, the face surface is the point of contact. For women, a larger surface area is involved…both legs. These use profiles present chronic exposure as well.

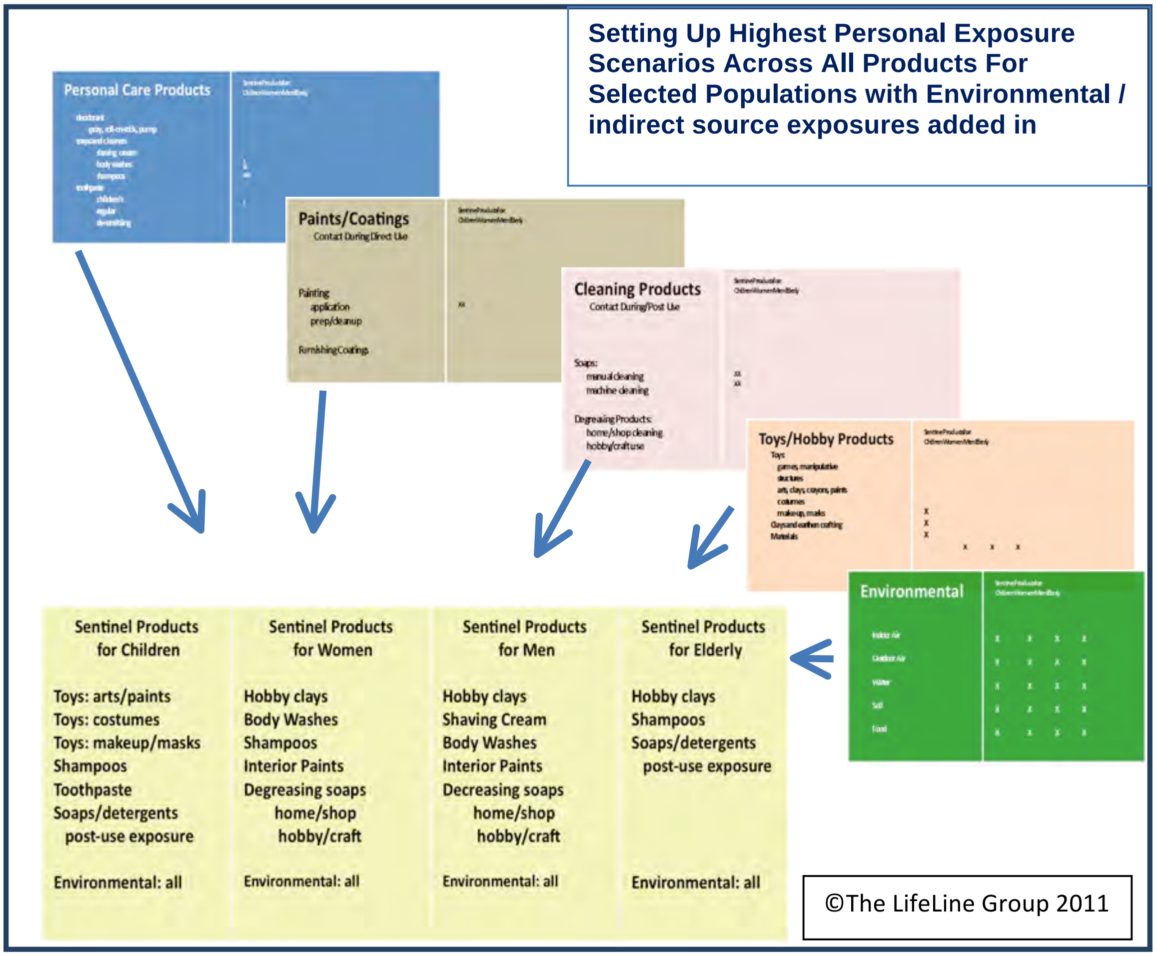
Seasonality also plays a role in the choice of Sentinel Products. This chemical is an important ingredient in some sun tan lotions. That product can be applied to whole body surfaces several times a day. Even though this may only occur for a few days a year, for those times, this is a significant exposure opportunity…for all ages. The concentration in sun block products varies greatly, but the highest concentration should be used for the assessment.

This process is continued for all of the Product Groupings for this chemical. If the chemical serves more than one function as a product ingredient, the process should probably consider each chemical function grouping separately since it is very likely that its occurrence probability and concentrations in products will differ depending on its ingredient function.

So, from the thousands of separate products containing this chemical, a much smaller set of Sentinel Products and use profiles will form the basis of the exposure assessment and relative ranking calculations.

After choosing Sentinel Products for individual product groupings, a set of Sentinel Products across all product groupings is accrued for each age group or special subpopulation. The accrual could look like the example below, with a different array of Sentinel Product for each subpopulation group.

Example: Surfactant A



Note here that the contribution from environmental sources can be included here for all subpopulation groups. Environmental exposure may result from air (intermittent, seasonal or long term), drinking water (consumed directly or used in food preparation), food, household water used in bathing or other activities, and dust/dirt both indoors and outdoors. The genesis of the exposure information from these environmental sources of the chemical is discussed below in the Environmental Prioritization (section 3), but by treating this exposure together with direct exposure from the Sentinel Products, we can consider the relative contribution of environmental sources in the overall exposure from the chemical.

2.4.4 Step 4: Relative Ranking by Prioritization Model

Prioritization modeling brings together the Chemical-Specific, Product-Specific and People Specific Information to yield a relative ranking of the chemicals based on their potential for adverse public health impact to any population group by exposure route. Also, for each chemical, the relative contribution by any one Sentinel Product or Environmental Source to overall exposure to a population group is calculated so those significant contributors can be highlighted as potential Priority Products.

The assessor informs the model as to the chemical's toxicity profile, physical/chemical characteristics, Sentinel Products, high-end concentration of the chemical in these products and similar product-specific information. Prioritization models [7] contain the "People Information" in the form of algorithms reflecting product use profiles for different ages and subpopulations and activity profiles important to the dynamics of personal exposure. For example, toddler's contact to carpeting would include skin surface area contact for some proportion of the day, hand-to-mouth events whereby chemicals from the carpet (or surface dust) could be transferred to the mouth, breathing rates and height/weight characteristics for different age groups, frequency and duration times for activities like sleeping, play time, etc. Model algorithms draw on the assessor-provided information for parameter values to calculate exposure—inhalation dose from airborne vapors or spray droplets, for example. The route-specific total dose from all of the Sentinel Products or sum of all routes of exposure is then compared to the chemical-specific toxicology metrics as appropriate. An adverse health effect "score" is calculated for each chemical and all chemicals are ranked – from those most likely to cause significant adverse health effects to least likely. Relative contributions by Sentinel Products and environmental sources are then calculated and ranked as well. DTSC would select priority products for Health from the sentinel products that make the greatest contribution to reducing a chemical's exposure and potential for adverse impact

The existing prioritization model would be updated to include current best-practices algorithms and activity scenarios for all product types in which candidate chemicals are used. That task starting with the accrual of the People – Specific Information is a one-time effort, useable for all subsequent chemical/product assessments. Of course, the model algorithms and underlying knowledge bases can be updated again in the future as the Department deems appropriate to incorporate better information as provided via notice and comment.

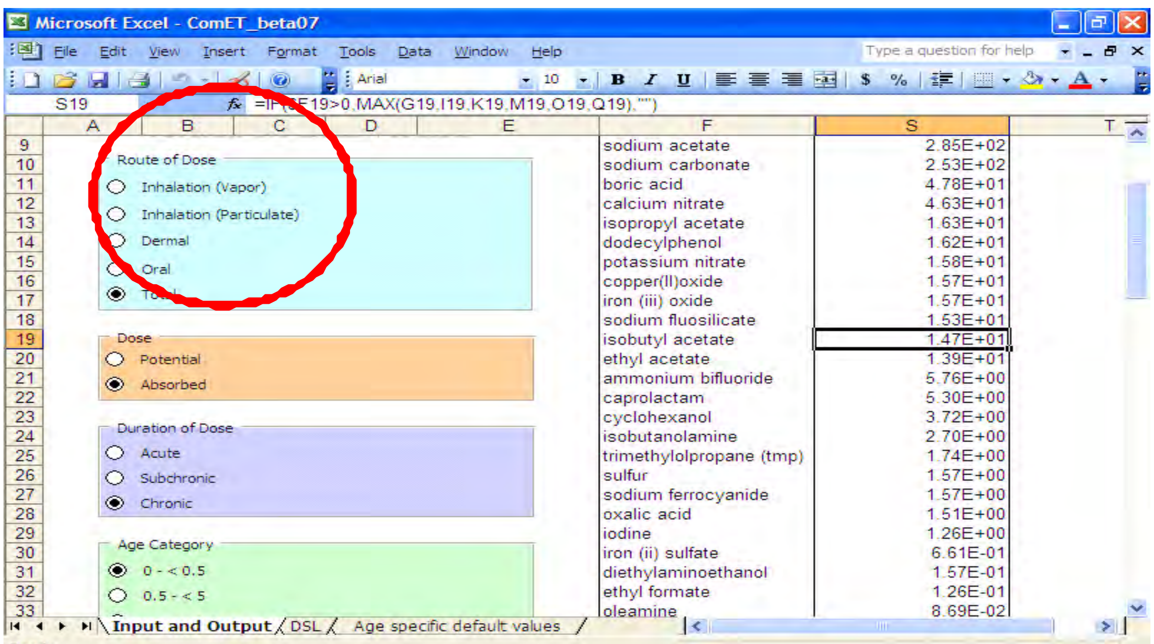
2.5 ComET tool

The ComEt© prioritization prototype model was used for the Canadian Model Peer Review in 2004-2006. Since then it has been expanded and the current version, also a proof of concept version, is CEPST™ , the Chemical Exposure Priority Setting Tool. It is freely available from www.TheLifeLineGroup.org.

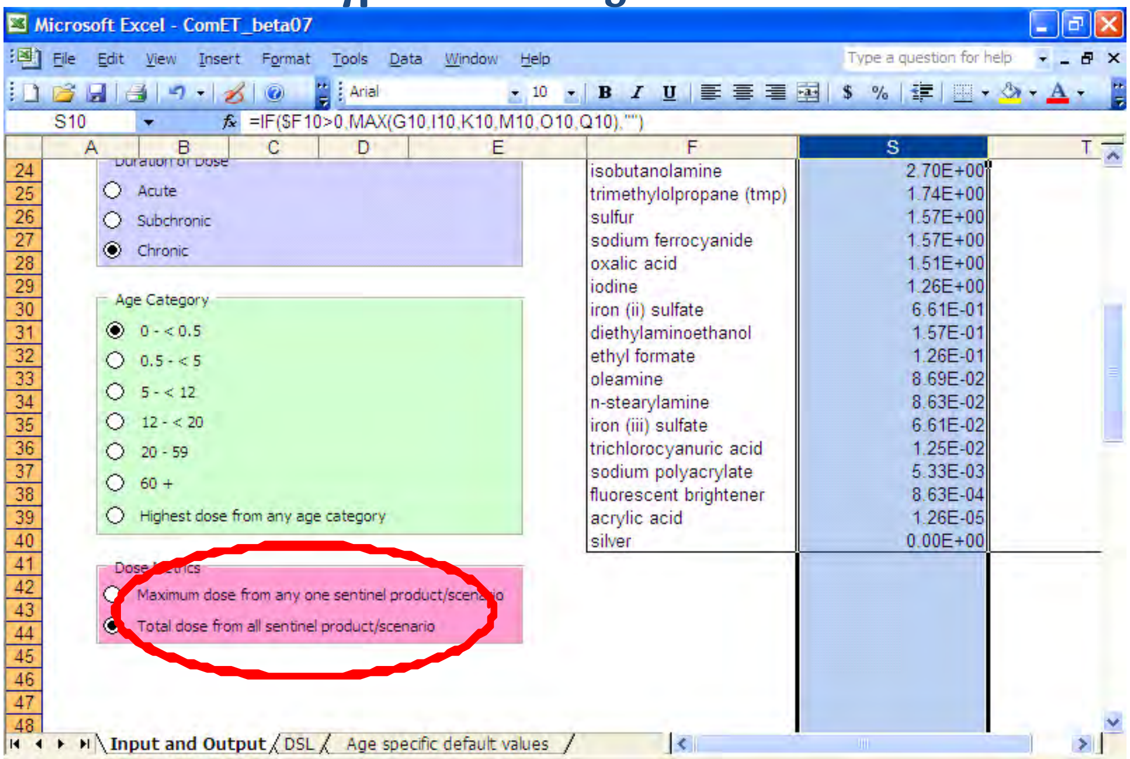
[7] The only prioritization model known to be designed and evaluated in a proof of concept test is the ComET™ model. Therefore, the operational logic and functions of that model form the basis of this description.

The following screen captures illustrate options for creating the ranking logic. Different ranking logic can be applied for a second and third tier of chemical prioritization. Ranking orders can be viewed by route of exposure, duration of exposure and across different age groups or special subpopulations. When chemicals fall high on the relative ranking in two or more of these ranking logics, justification is strengthened for enhancing the priority of those chemicals.

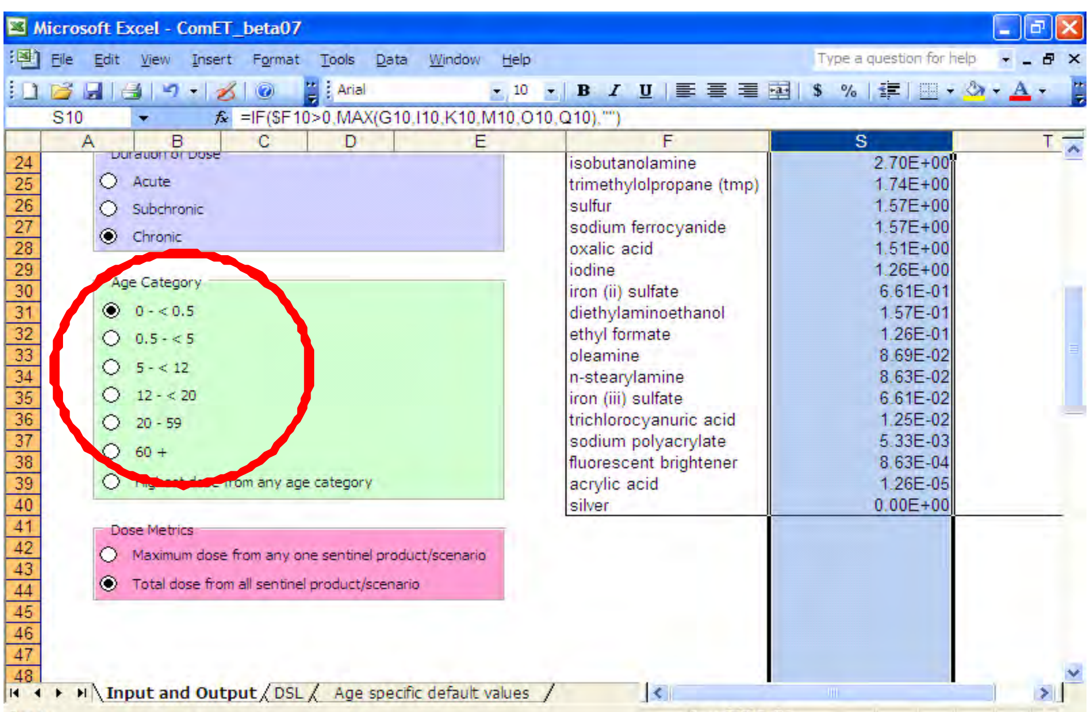
Ranking by Route of Exposure



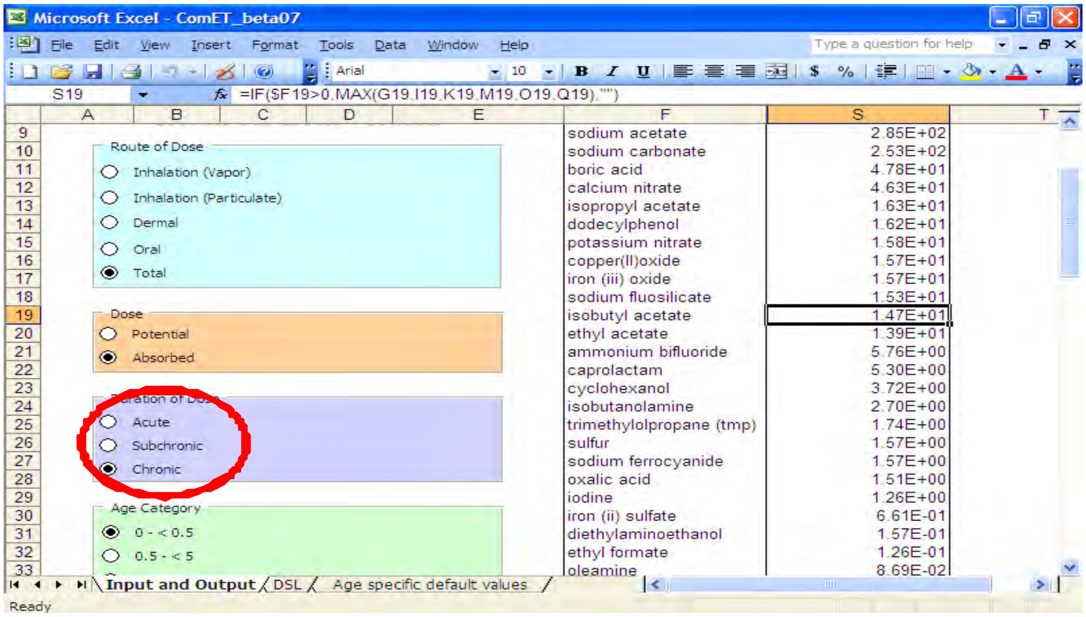
Type of Ranking Exercise



Ranking Exposures within Age Groups



Ranking by Duration of Exposure



Note that the quantitative ranking metrics shown in these screen captures reflect the use in the exposure-only basis designed for Canada. Although calculated exposure values are shown here along with the relative rankings, those values are not useful independently as predictive exposure assessments (for all the reasons previously discussed). A ranking is accomplished by selecting the type of exposure situation of interest, and age group. Since different Sentinel Products represent the exposure opportunities for different age groups (true for most chemicals), obviously different relative rankings across chemicals will emerge depending on the age group being considered. DTSC would select priority products for Health from the sentinel products that make the greatest contribution to reducing a chemical's exposure and potential for adverse impact.

The chemical rankings shown above were part of the Health Canada Model Peer Review discussed in the next section.

Using the logic described above, the metric for DTSC's regulation would be a relative adverse impact score obtained when the chemical's exposure is compared to the appropriate toxicology metrics.

2.6 Highlights of Similar Process in Canada

The quest for assuring public health and environmental safety has encompassed multiple forms of legislative initiatives directed toward consumer products and the chemicals in those products. To implement the Canadian Environmental Protection Act (CEPA) Health Canada and

Environment Canada employed a process considering the potential health and environmental consequence of these chemicals in consumer products. Health Canada utilized an initial step of prioritization considering both potential hazard and potential exposure.

- Health Canada prioritized chemicals with the greatest potential for exposure, also with an eye toward eventual substitution for the highest concern uses of chemicals in products. The initial phase (through 2006) of prioritization was accomplished through separate parallel programs considering toxicity (hazard potential) and exposure. No prioritization models existed at the beginning of this task. Canada developed a hazard ranking decision-matrix and an exposure-based prioritization tool (ComEt) which it used as a proof of concept and employed its principles. After completing prioritization, Health Canada then initiated chemical-by-chemical predictive screening assessments for the highest priority chemicals.

The prioritization approach presented in this document, using a relative ranking model and Sentinel Products, was designed and tested by The LifeLine Group commissioned by Health Canada as part of the work leading to the first wave of chemical prioritizations under the Canada Environmental Protection Act. This approach was subjected to a **"Proof of Concept" Trial** as described below.

Task: For approximately 200 chemicals, identify uses of the chemicals in consumer products and create a relative ranking of the potential exposure to various age groups of the population. Although Health Canada had some industry-supplied information about the uses in commercial products, this Trial could utilize only publicly available information obtained independently.

The use profile information gathered by The LifeLine Group was compared to the industry information existing in Health Canada files prior to 2005. The entire process, including logic for choosing Sentinel Products, was presented publicly by Health Canada. [8]

Using the prototype relative ranking tool, ComET, the approximately 250 chemicals were ranked.

2.7 Practical Considerations and Lessons Learned

Practicality is a theme in implementing the statutory mandates. Clearly, the intent of the legislation and regulation is for meaningful progress toward safer environments and consumer products. This goal must be accomplished within the realities of Department resources and must encourage constructive participation by all stakeholders.

[8] ComET Peer Input Meeting: Context & Objectives, Bette Meek, Health Canada, Nov. 8th, 2004, TERA Peer Review Meeting, Cincinnati, Ohio, Nov 8, 2004.

Using those ideals as markers of "practicality", we can examine the proposed process and consider the lessons learned from the Canadian experience with this approach.

First, a reflection on the experience using this approach to date:

2.7.1 Lessons Learned.

1. Information gathering, choice of Sentinel Product and initial use profiling requires 4 hours or less for most chemicals.

2. Public availability of needed information is expanding, spurred by other regulatory initiatives, transparency requirements, nationally organized public databases, and industry's evolving willingness to release commercial information.

3. Scientists and regulators initially underestimated the sources and extent of publicly available information available about chemical uses, product characteristics, use profiles, ingredients and other parameters involved with these assessments. Skepticism always surfaces about this issue when first introduced.

4. Exposure scenarios for products are "reusable" across many chemicals, so efficiency increases as the process continues.

5. Established criteria and a decision matrix greatly aid the deliberation for choosing Sentinel Products, enhancing consistency of approach and minimizing assessor bias.

6. Structured and disciplined processes are highly advisable for several aspects of the prioritization approach including:

    a) Search strategies for Chemical Specific and Product Specific information,

    b) Choice and application of default values, assumptions, surrogate data, etc.,

    c) Categorization of products,

    d) Selection of Sentinel Products,

7. Focus on critical points of the process for quality control (expert oversight).

Appropriate training and oversight of assessors will enhance the credibility of the process, as would be true for any new process for regulatory purposes. Credibility of the approach and its conclusions is enhanced with consistency of approach, understanding the assessment options, and structured, transparent deliberative approaches. . That credibility will encourage constructive participation by stakeholders. It is also vital that the prioritization model and underlying knowledge bases be publicly and freely available to all interested parties. This provides opportunity for scientific review, development of improved information and model algorithms as well as increased confidence in the regulatory process overall.

2.7.2 Practical Considerations of the Approach

The approach presented here is both responsive to the legislative intent AND practical.

Prioritization based on the potential for exposure and adverse health impacts can be accomplished in a time and cost-efficient way. However, there are some topics which are especially important to the fulfillment of the opportunity to efficiently and effectively execute the goals of the legislation and guidelines of the regulation. A brief summarization of those follows:

- Selection of Significant Hazard Endpoints – Department policy

For coherent prioritization, metrics for potency of a chemical should be relevant to significant human health threats. This first step, which sets up the candidate chemicals based on hazard potential, could rely on CMRs or similarly significant health endpoints.

- Selection of model algorithms, underlying default data and population activity profiles. – Setting up the prioritization model and subsequent peer review.

Assessment tools exist but underlying assumptions, algorithms and default parameters need expansion and upgrading with information appropriate for the chemicals and products under consideration by the Department. That up-front task yields a transparent model construct easily presentable for peer review and use by all interested parties. DTSC can utilize existing information sources and structured elements available from a variety of credible sources.

The prioritization approach presented here is new but not difficult. Like any new process, it will require some training, practice, process standards and good quality assurance oversight to yield good regulatory results.

The prioritization approach yields a clear "conclusion" in ranking chemicals and the products in which they are used, enabling DTSC to propose science-based chemical and product priorities within available resources.

3. Environmental Prioritization

The Green Chemistry Legislation in California has, as its purpose to establish a prioritization process to determine which chemicals in consumer products should be given priority for alternatives assessment. As shown in Figure 1, the identification and prioritization process starts with development of a set of candidate chemicals for prioritization based on volume, potential for exposure and hazard properties and other information indicating the potential for significant impact on public health and the environment (e.g. CMRs and PBTs), especially sensitive subpopulations. After this set of chemicals is identified, the next step is to prioritize them to develop:

- a relative ranking for the environment based on potential for adverse environmental impacts to organisms in the environment; and,
- a relative ranking for health based on overall exposure including indirect human exposure to these chemicals after their release to the environment as a result of use and end-of-life disposal.

The adverse impact on the environment will be based on a screening level environmental exposure and impact assessment, which uses information on the volume of the chemical used in California and released to the environment to calculate exposure and information on toxicity values to determine the potential for impact on the environment and representative higher trophic level organisms of interest to the Department. These higher trophic level organisms could be chosen to represent, for example, raptor birds (e.g., eagles) where exposure would result not just from direct contact with the chemical in the environment but also could occur through the food chain by consuming food that contains the chemical of interest. The environmental exposure to the population from the environment will be estimated as the exposure through air, food, and water which will be added to the direct exposure from consumer products discussed previously to determine an overall exposure for the health ranking.

3.1 Candidate Chemicals: Environmental

The proposed regulation indicates that the identification of candidate chemicals for environment should focus on PBT chemicals because these characteristics when taken together are an indicator of potential for presence of the chemical in the environment, plus its ability to get into an organism where it can cause adverse impacts. These are also the types of chemicals that can cause concern for exposure to higher trophic level organisms through the food chain.

The recommended process for identifying PBT candidate chemicals that are used in consumer products would follow the following steps

1) Develop a global set of PBTs based on authoritative body sources
2) Compare these chemicals to the most current US EPA Inventory Update Report (IUR) compilation to determine if these PBTs are manufactured or imported into US commerce
3) Determine which of these PBTs in US commerce are used in consumer products.

In choosing which PBT sources can be considered authoritative, the sources should meet certain criteria including: developed by authoritative government bodies; use the same internationally accepted cutoff values for the characteristics; conducted in an open, deliberate and transparent process with ample opportunities for stakeholder participation and feedback; widely perceived to be objective; and scientifically based including having undergone and continue to undergo public comment and review and using the best science available including the incorporation of multiple lines of evidence within a weight-of-evidence approach. Finally, the characterization and guidance documents are publicly available, and the categorization is subject to on-going review as new data and approaches are developed. Sources that meet these criteria include the US EPA's TRI and Waste Management PBTs[9], Canada's Priority PBTs[10], the European Union's PBTs and Substances of Very High Concern – PBTs[11], and finally the UN LRTAP and Stockholm Conventions[12]. Building from these other efforts, which have taken many years to accomplish, will provide a set of initial candidates in a time effective manner. One caution is that within some of these programs, there are a few currently proposed PBTs which are undergoing extensive public comment and review such that some of these chemicals may be found later to not meet the PBT criteria. Thus, these very few chemicals should not be included in the initial candidates until the reviews are complete to avoid entering into debate, which could focus the effort away from the main goal of the regulations.

[9] http://www.epa.gov/tri/trichemicals/pbt%20chemicals/pbt_chem_list.htm and http://www.epa.gov/osw/hazard/wastemin/priority.htm

[10] http://www.ec.gc.ca/lcpe-cepa/default.asp?lang=En&n=5F213FA8-1&wsdoc=D031CB30-B31B-D54C-0E46-37E32D526A1F

[11] http://echa.europa.eu/chem_data/authorisation_process/candidate_list_table_en.asp and

http://echa.europa.eu/consultations/authorisation/svhc/svhc_cons_en.asp

[12] http://chm.pops.int/Convention/The%20POPs/tabid/673/language/en-GB/Default.aspx

The second step is to compare this initial set of global PBTs with the most current US EPA IUR information[13] to determine if the PBT chemical is manufactured or imported into US commerce. The IUR is updated on a regular basis and is expected to be conducted in 2011.

Finally, the set of global PBTs in US commerce that are used in consumer products can be determined using the approach is discussed in detail in the previous Health Prioritization description.

Once this set of global PBTs in US commerce that are also used as ingredients in consumer products is determined then these candidates will then enter into the environmental prioritization as shown in Figure 1.

3.2 Overview of Prioritization

There are two types of environmental exposure that need to be considered in the first step of the prioritization, which focuses on prioritizing the candidates as shown in the chemical ranking framework in Figure 1. First there is exposure to environmental receptors such that there could be adverse impacts on the environment. This exposure and potential for adverse impact on the environment is used to develop the environmental ranking of the environmental candidates. The second type of environmental exposure is indirect or secondary exposure to the population through the environment, which includes air, water and food sources. This second type of environmental exposure will be used in conjunction with the direct exposure from consumer product use to inform the Health ranking (Section 2.4.3) and thus would be conducted for chemicals that are of concern for health based on CMR or other health concerns.

In the second step of the environmental prioritization, product ranking framework of Figure 1, the focus is on identifying and prioritizing consumer products that contain the proposed chemicals of concern. This step in the prioritization builds on the exposure and impact assessments conducted in the first step of the prioritization for chemical ranking based on environmental impact. The result is a ranking of products that use the proposed chemicals of concern based on the environment impact.

3.3 Prioritization based on Adverse Impact on the Environment

As a result of product use or end-of-life disposal practices for consumer products, there is a potential for release into, migration among and distribution of the chemicals of concern across environmental media such that exposure to environmental receptors can occur. Therefore, the first step in developing a ranking and prioritization based on adverse impact on the environment involves estimating environmental exposure concentrations in California. This screening level exposure, which would be based on the volume of chemical used in California

[13] http://www.epa.gov/iur/tools/data/index.html

and the fraction of this volume released to the environment, would represent an average concentration in California for the environmental media and include exposure to representative higher trophic level organisms of interest to the Department. To develop the ranking based on adverse impact on the environment, these environmental exposure concentrations both in the media and higher trophic level organisms are compared to appropriate environmental toxicity endpoints. The ratio of the toxicity endpoint to the exposure concentration can be used to rank the potential for adverse impact with the higher the value of this ratio indicating the higher the priority for that chemical.

The volume of the candidate chemicals in California can be initially estimated from IUR volumes[14] using a factor representing the percent of the US population that reside in California for example, approximately 12% based on the 2009 census. This can be refined as appropriate based on the information collected as discussed in the health prioritization section. Also, any environmental management practices such as waste treatment or containment or product properties such as presence of chemical in article that will reduce the amount released to the environment would be considered.

The appropriate environmental toxicity information can be determined using several authoritative and publically available databases such as: 1) ECOTOX database[15], 2) REACH chemical registrations[16], 3) OECD HPV program submissions[17], 4) US HPV program submissions[18], and 5) US EPA chemical data access tool[19]. There are also QSAR tools, such as the US EPA's EpiSuite[20], that can be used to estimate any missing toxicity data. A final compilation of the appropriate databases and the search scheme will be developed as the guidance based on these recommendations is further developed.

The environmental exposure concentration can be estimated using an environmental exposure model that provides these exposure concentration estimates based on California environmental

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[14] http://cfpub.epa.gov/iursearch/index.cfm?err=ch&term=1322981

[15] http://cfpub.epa.gov/ecotox/

[16] http://apps.echa.europa.eu/registered/registered-sub.aspx

[17] http://www.echemportal.org/echemportal/index?pageID=0&request_locale=en

[18] http://www.epa.gov/hpvis/

[19] http://java.epa.gov/oppt_chemical_search/

[20] http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

characteristics, the volume of the chemical released to the environment in California and the physical-chemical and degradation properties of the chemical. Whatever tool is used, it should be selected based on a transparent set of criteria including being well recognized and currently accepted by the environmental community as a fate and exposure model, fully documented and publically available, currently is or can be parameterized for California environment, and includes the endpoints of interest to DTSC including the ability to estimate exposure in representative higher trophic level organisms of interest to the Department.   In addition, the model must be able to handle a large number of chemicals in a batch mode and report the results in a form that will allow for informing the ranking similar to the capabilities shown for the ComET tool previously.

There are several existing models that could meet this need with little additional effort to modify or update the underlying data and algorithms, including the CalTOX model[21] that was previously developed for and used by DTSC to evaluate waste management options, the RAIDAR model[22] and the EUSES model[23] used by the European Commission in their chemical evaluations. The RAIDAR model has been used to inform Canada's environmental prioritization of the chemicals and has shown to be an efficient and effective tool for chemical prioritization[24]. The current version contains many updated features and algorithms compared to the CalTOX model.

This figure shows pictorially the environmental fate and exposure components of the RAIDAR model and illustrates the needs to be considered in developing the criteria for choosing the tool and the importance of including a full suite of the environmental fate properties and processes as well as exposure to higher trophic level organisms, illustrated by the eagle and wolf.

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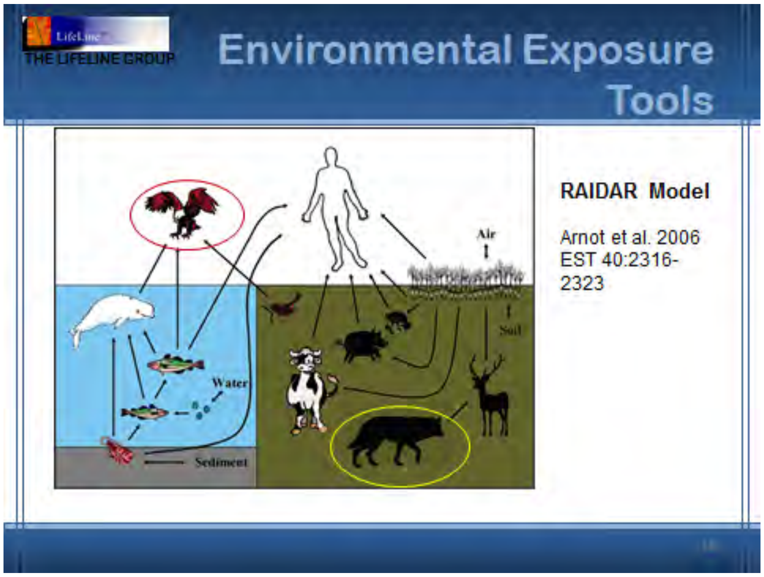
[21] http://www.dtsc.ca.gov/AssessingRisk/caltox.cfm

[22] http://www.trentu.ca/academic/aminss/envmodel/models/RAIDAR100.html

[23]

http://www.pbl.nl/en/publications/2004/European_Union_System_for_the_Evaluation_of_Substances_2_0__EUSES_2_0___background_report

[24] Arnot et al. 2006 Environ. Sci. Technol. 40:2318-2323, and 2008 Environ. Sci. Technol. 43:4648-4654

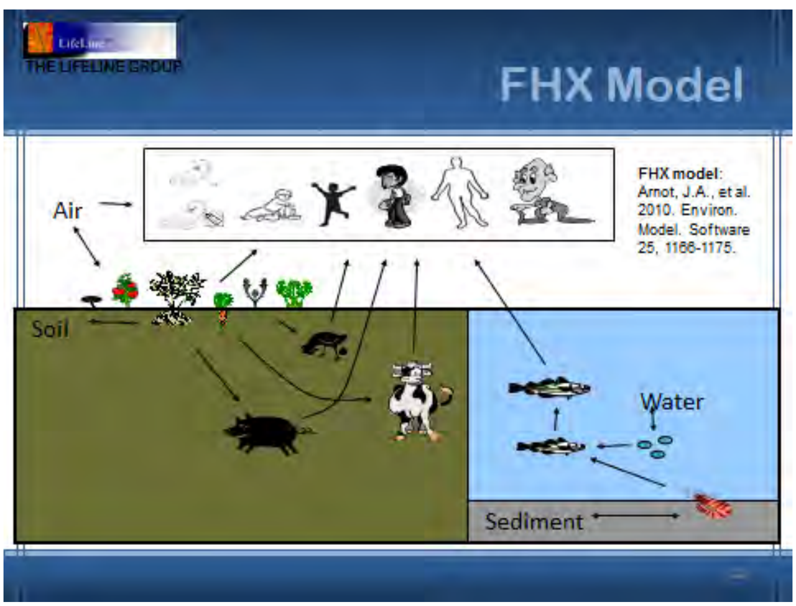


3.4 Prioritization based on Environmental Exposure to Population

The health ranking and prioritization for the CMRs and other chemicals of health concern that have been identified as candidate chemicals for the health prioritization, must consider the indirect exposure through the environment, in addition to the direct exposure to the chemical from consumer product use. As recognized in the regulations, there is a potential for consumers to be exposed to the candidates through environmental media including water, air, and food in which the chemical is found due to release to the environment as a result of product use or end-of-life disposal. This environmental exposure is combined with the direct consumer product exposure discussed previously to complete the ranking for prioritization for human health as shown in the chemical ranking framework in Figure 1.

The exposure information needed to estimate this indirect exposure to the population and individuals in the population are the concentrations in primary media of air, water and soil and the resulting concentrations in various food items which is estimated from the flow of the chemical from the environment and through the food chain based on the amount of the chemical used in California and released to the environment and the physical-chemical and degradation properties of the chemical. These concentrations are combined with information on the intake of the various types of foods by the population and various representative subpopulation groups to estimate the indirect exposure. These groups would be chosen to match the groups used in the health assessment so that the two exposures can be added transparently.

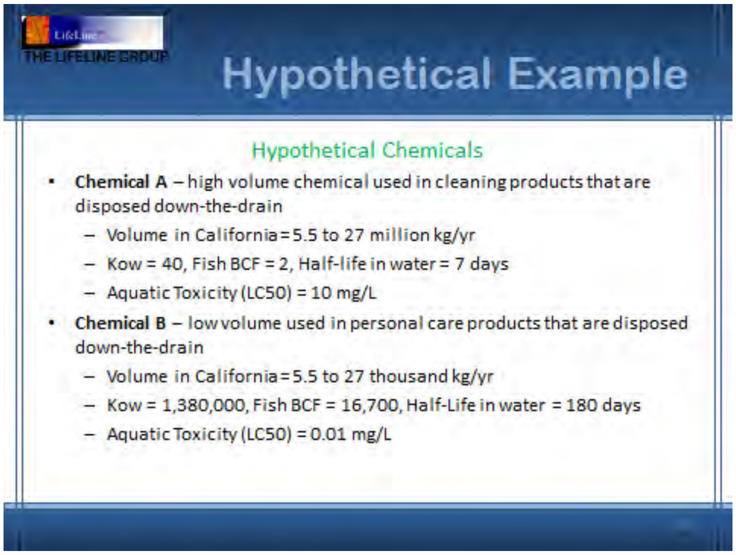
As with the environmental exposure assessment described previously, several models currently exist that could be used to provide an estimate of the exposure from the environment to the population, if properly parameterized for the California environment and California population exposure characteristics. The first step in choosing such a tool will be developing criteria based on the needs of DTSC and the regulatory objectives. Ideally this model would be integrated with the model that is used to estimate the environmental exposure concentrations as these represent the exposure through the environment to the population from drinking water and air. Criteria that could be considered in choosing the tool are similar to the ones used for choosing the environmental exposure model, including that the tool is well-recognized and accepted, fully documented and publically available. Specific considerations for this tool will be the presence or ability to incorporate the exposure to the full population and to subpopulations of specific interest to DTSC. Some of the potential tools/models that are available include the ones identified for the environmental exposure such as CalTox which includes some elements of population exposure, RAIDAR which currently includes exposure to a representative person in the population as shown in previously and EUSES. In addition to these models, the FHX model[25] which uses the same environmental fate and food chain models but estimates the exposure to various subpopulations as illustrated in the following figure should be considered. In all cases the choice of the final model/tool to use must consider the ease of modification to include the California population characteristics including food intake patterns, the ability to estimate exposure to the population and specific age groups of interest as well as ability to have the resulting exposures easily integrated with the tool used for health ranking.



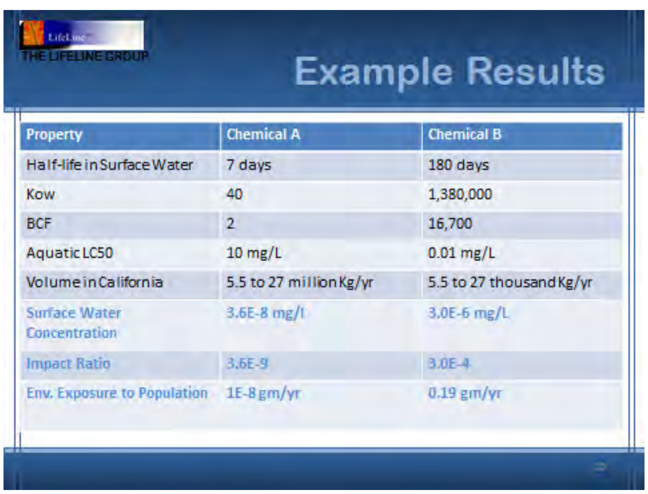
3.5 Illustration of Environmental Ranking

The chemical ranking is illustrated by comparing two hypothetical chemicals whose properties are shown in the following figure.

[25] Arnot, J.A., et al. 2010. Environ. Model. Software 25, 1166-1175



The resulting adverse impact ratio (shown on following figure) shows that in terms of environmental ranking, Chemical B would have priority (higher rank) based on the adverse impact ratio than Chemical A because of the higher exposure concentration. This illustrates that volume alone could lead to misleading ranking of the chemical because the volume of Chemical A is much greater than the volume of Chemical B and that PBT characteristics will be important in the environmental ranking, because Chemical B is categorized as a PBT whereas Chemical A is not a PBT. The Environmental Exposure to the Population would be combined with the Sentinel Product exposure as described in Section 2.4.3 to generate a total exposure to that chemical to inform the health ranking.



Property	Chemical A	Chemical B
Half-life in Surface Water	7 days	180 days
Kow	40	1,380,000
BCF	2	16,700
Aquatic LC50	10 mg/L	0.01 mg/L
Volume in California	5.5 to 27 million Kg/yr	5.5 to 27 thousand Kg/yr
Surface Water Concentration	3.6E-8 mg/l	3.0E-6 mg/L
Impact Ratio	3.6E-9	3.0E-4
Env. Exposure to Population	1E-8 gm/yr	0.19 gm/yr

3.6 Product Prioritization for Environmental

The second step in the prioritization is to develop a ranking for the consumer products in which the proposed chemicals of concern are used and is shown in the product ranking framework in Figure 1. This process uses the information from the previous chemical of concern prioritization as well as information on the releases to the environment from the various types of consumer products within which the chemical of concern is used. Thus, the key new piece of information needed is the relative proportion of the total chemical volume used in California that is used as an ingredient in different types of consumer products and the fraction of this volume released to the environment. Since this does not need to be an exact number but rather a relative proportion, these proportions could be estimated from market volumes of the various product types factoring any significant differences in the percent of that chemical in the specific product type and the potential release from the product to the environment. This percent in product type information will have been gathered in the health ranking (section 2.3.2). Those products that contribute the most to the volume of the chemical released to the environment would have the highest ranking for environmental impact. DTSC would select from this ranking priority products for the Environment that make the greatest contribution to reducing the volume and exposure of the chemical released to the environment and its potential for adverse impact.

3.7 Summary of Environmental Prioritization

As described above, it is possible with reasonable effort and time to develop both a set of candidate PBT chemicals for prioritization, to conduct the first step of the prioritization of these chemicals based on their potential for adverse impact to the environment and to conduct the second step of the prioritization in ranking priority products that use the chemicals. It is equally reasonable to inform the health ranking by providing an estimate of the indirect exposure to the population and representative subpopulations from the environment.

4. Concluding Remarks

Relative ranking can accomplish the objectives of chemical and product prioritization for health and the environment. The identification and use of Sentinel Products in the health prioritization provides a practical and efficient approach to focus the work on the most important sources of potential exposure and adverse impact. The integrated process described is objective, science-based, meaningful, and transparent. It produces rankings based on quantitative comparisons of hazard and exposure, addressing both human health and the environment. It is responsive to the statute's requirements to consider volume, potential for exposure and sensitive subpopulations and complies with California's Administrative Procedures Act. It leverages existing, publicly available data and can deal with hundreds of potential chemicals of concern and thousands of products. The relative ranking outcome enables addressing the highest and most critical adverse impacts first. The number of chemical and product priorities selected would be dependent upon available departmental resources. Results as well as underlying assumptions can be made transparent, and improved through public notice and comment. This approach has been tested and found to be useful in meeting the objectives of Canada's prioritization under the Canadian Environmental Protection Act